

**TITLE OF PROJECT: EARLY INTERVENTION TRIAL FOR VISUAL PROCESSING
DEFICIT IN CYSTINOSIS**

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Hypothesis: Children with cystinosis will improve their visual processing skills by repeated, graded presentations of visual stimuli.

Specific Aims: To determine whether a unique program of computerized visual stimuli, presented in slowly increasing speed of presentation and complexity, will improve visual processing in children with cystinosis.

Progress Report/Summary of Study Results:

Background: In earlier studies, we found that children and adults with nephropathic cystinosis often have significant difficulty with visual spatial skills, and that this in turn can lead to academic difficulties, particularly with math. Earlier studies by Bernhard and Major (2005) and Temple et al. (2003) had demonstrated that a computerized program of gradually increasing difficulty could help to improve auditory processing speed in children with language-based learning disabilities. We hoped that we could use a similar idea to improve processing of visual information with a computerized program that would gradually increase visual processing speed.

Methods: We identified an appropriate computerized cognitive rehabilitation program (NeuroPsychOnline; NPO) and trained a staff research associate on all the cognitive testing, as well as the intervention program. We then attempted to enroll subjects for the study. Our target population was school-aged children with cystinosis. These children received baseline cognitive testing as well as follow-up cognitive re-testing every 3 months for a 9-month period (for a total of 4 cognitive testing sessions). An intervention trial took place between either the first and second testing sessions or the second and third testing sessions. The 12-week intervention trial was initially 1 hour per day, 5 days per week, of on-line work using the cognitive rehabilitation program. Since these children were from various parts of the country, the research associate initially traveled to their homes for testing, trained the child and parent on how to use the on-line program, and then remotely monitored use of the program by when the child logged on and for how long. We quickly determined that there were major problems with the study. Parents were busy and it was difficult for them to monitor their children to insure compliance. The children did not like spending one hour per day doing the exercises. Non-compliance was a major problem. Because of this, we modified the study such that the children were only required to log on for ½ hour daily for 5 days per week

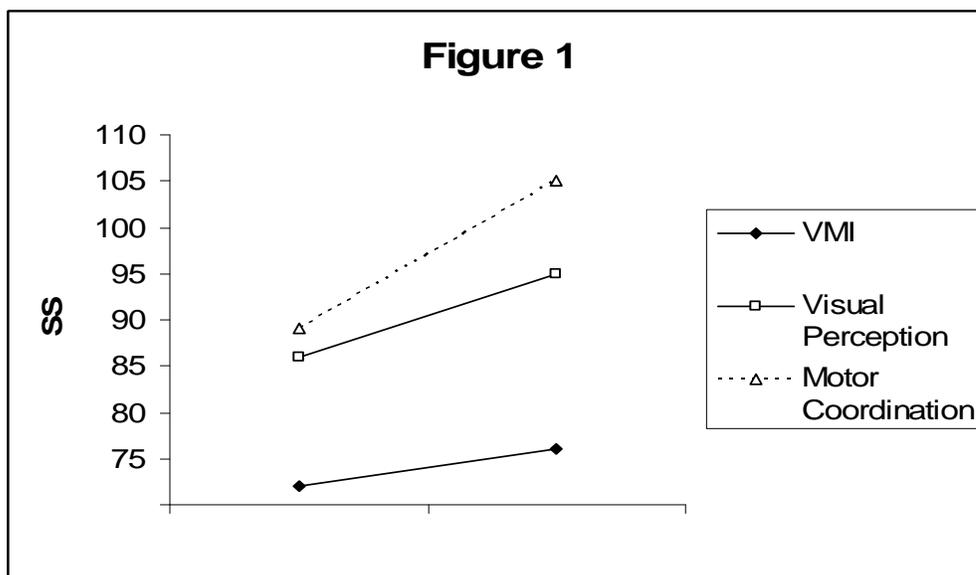
Results: To our surprise, despite great interest expressed by many families to help their children improve academically, both recruitment and compliance proved challenging. More than twenty families were contacted directly about the project and advertisements were placed in key locations (e.g., the Cystinosis Research Network website and the CRN listserv); despite these attempts, only 8 participants agreed to enroll in the study. Once enrolled, furthermore, a number of these participants did not complete the computerized intervention program (NPO) on a regular

basis. In order to monitor and increase adherence, each day we tracked whether participants were logging onto the NPO. If they were not logging on regularly, we contacted the participants' parents to inform of the participant's progress and to ask whether they were having questions or problems with the computer exercises. We emphasized the importance of doing the exercises on a regular basis, stressing that any potential benefits of the exercises would only occur if they were completed regularly. We also sent cards with stickers in them congratulating participants when they had logged on regularly and encouraging them to keep up that pattern. Additionally, we worked with the parents and children to schedule specific times and dates when the children would log onto the program. We then periodically contacted the families at the scheduled times if the child was not logged on at the time.

Despite these efforts, adherence to the computer-based exercises was extremely low. As mentioned above, in an attempt to increase adherence, in May 2006 we amended the protocol to reduce the amount of time participants spent doing the computer exercises. Specifically, instead of spending 60 minutes per day, 5 days per week, the new procedures required participants to spend 30 minutes per day, 5 days per week. In addition, we began offering a modest payment to participants for their participation in the intervention phase of the study (in addition to the payment they received for each of the testing sessions). Although these changes appeared to improve adherence modestly, the majority of participants still did not work on the computer exercises on a daily basis.

Finally, one participant withdrew from the study after one week of participation. The participant logged onto the NPO exercises 5 times during that week, and then the participant's mother reported that the participant found the exercises to be stressful, despite the fact that the mother emphasized that the participant was not receiving a grade for the exercises and that merely working on the exercises was the goal.

Given the problems associated with participation and compliance, our results, although provocative, are somewhat limited. Between baseline and immediate post-treatment testing, there were improvements in scores on standardized tests of Visual Motor Integration (VMI), Motor Coordination, and Visual Perception (see Figure 1). The Motor Coordination test reached significance (Repeated Measures ANOVA, $p = .02$). The standard scores changes in VMI and Visual Perception over time did not reach statistical significance, likely because of the small number of participants.



Given our previous research showing deficits in individuals with cystinosis in the area of Visual Motor Integration (Scarvie *et al.*, 1996), these limited results are intriguing. These results suggest the potential of an intervention program to improve performance in cognitive domains previously documented to be weaknesses for individuals with cystinosis.

Self-Concept in Cystinosis

Before beginning the intervention, participants were administered the Multidimensional Self Concept Scale (MSCS; Bracken, 1992). This questionnaire is completed by the child and assesses self-concept in the most important contextual or environmental domains for children and adolescents, and was theoretically devised and empirically supported (Bracken, 1992). Self-concept is a multidimensional behavior pattern that reflects an individual's evaluation of behaviors and experiences, influences current behaviors, and predicts future behavior. Given the complexities surrounding living with cystinosis (both the positive and the negative), we believe that a greater understanding of self-concept in individuals with cystinosis is warranted, as this is a construct that has not yet been examined in children and adolescents with cystinosis.

The MSCS is designed to assess self-concept on a number of different domains. Specifically, the participants were asked numerous questions about how they perceived themselves on the following dimensions: social, competence, affect, academic, family, and physical. The participants' scores were compared to the scores for a large, nationally representative normative sample in order to determine how similar the self-concepts of the children in our study were to those of "typical" children.

Despite the numerous challenges that children with cystinosis can face, the participants in our study reported average self concept scores (note that the sample size for these analyses was very small (n=8), so results should be interpreted with appropriate caution). Specifically, on each of the 6 dimensions that were assessed, as well as on overall self-concept, our participants' scores were similar to those of the national sample (or in fact very slightly more positive than the national sample). For instance, despite the fact that children with cystinosis often encounter some physical obstacles, the children in our study did not have a negative Physical Self-Concept. The fact that our participants' self-concepts do not appear to have been adversely affected by the difficulties posed by living with a chronic illness is encouraging news, and future research should investigate the factors that may contribute to this resiliency.

Conclusions:

This study has led to several important conclusions. First, it is not likely that the proposed intervention will be generally useful in improving visual processing skills in children with cystinosis because of the difficulty in finding the time or the commitment to complete the intervention successfully. Thus, it will be important to search for different methods to achieve the desired goals. Second, despite the limited number of participants, there is some indication that such an intervention may be helpful in improving both visual processing skills and academic performance. Therefore, a search for a more efficient and user-friendly approach to remediation will be very important. If such a method can be identified, it is likely to be helpful in improving academic performance in those children with cystinosis who have educational challenges. Perhaps one solution would be to incorporate an intervention into the child's school day such

that he or she would receive the benefit of intensive cognitive training without its interfering with other after-school or weekend routines. We hope to pursue this possibility in future studies.

Overall this project was extremely informative in that it demonstrated how difficult it is to place additional demands on families that are already coping with chronic illness. Despite the fact that children with cystinosis have documented cognitive and academic difficulties, and that numerous families have inquired about potential interventions for their children, both recruitment and adherence posed significant problems. Although we were unable to conclusively demonstrate improvement with the intervention program, our results are provocative in that there is some indication of improvement despite less than optimal participation. It is possible that greater time spent on the computer exercises would indeed lead to the improvements we had hoped to see. Interestingly, although cystinosis is associated with documented cognitive difficulties, these difficulties may be perceived by families to be mild enough that they do not warrant spending the extra time required for a home-based intervention of this sort. Furthermore, the positive self-concept reported by the individuals with cystinosis may be one potential reason for the children not wishing to participate in the study; i.e., if they believe they are doing well, there would be no reason for them to choose to participate in a study that requires a significant time commitment.

References

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